

## **Extremely low prevalence of erythromycin-resistant *Streptococcus pyogenes* isolates and their molecular characteristics by M protein gene and multilocus sequence typing methods**

### **ABSTRACT**

Background: Group A streptococci (GAS) are notorious bacteria causing a wide variety of clinical manifestations ranging from mild, acute streptococcal pharyngitis to chronic non-suppurative diseases and immunological sequelae. They are further complicated by the global rise on the emergence of macrolide resistance among these bacteria in which several M protein gene (emm) and sequence types are associated with invasive diseases. Objectives: The current study aimed at determining the erythromycin resistance patterns and molecular characteristics of GAS clinical strains by emm and multilocus sequence typing (MLST) methods. Methods: Thirty-five GAS clinical isolates were subjected to antibiotic susceptibility testing by disk diffusion method. The minimum inhibitory concentration (MIC) of erythromycin against GAS by E-test was determined. Clinical and laboratory standards institute (CLSI) guideline was used for the interpretation of results. Detection of *ermA*, *ermB*, and *mefA* genes by polymerase chain reaction (PCR) was performed and emm typing was done by amplification and sequencing of emm genes per standard protocol. Allele and sequence type (ST) of GAS were obtained using the *S. pyogenes* MLST database. Results: All the isolates were sensitive to erythromycin, penicillin, clindamycin, chloramphenicol, and vancomycin (100%). Resistance to tetracycline was 54.3%. The *mefA* gene was found in one erythromycin susceptible isolate. No other erythromycin resistance genes were detected in the isolates. Twenty different emm types were found and the most frequent emm types/subtypes detected were emm1, emm18.21, emm28.5, emm97.4, and emm102.2 (each 8.6%). However, no new emm type was detected. A total of 15 sequence types (STs), eight clonal clusters (CCs), and eight singletons were identified among 21 representative isolates. Three isolates exhibited CC1 (ST28/emm1). Conclusions: High susceptibility of GAS isolates against erythromycin could be due to low antibiotic selective pressure in Malaysian clinical settings. High diversity of emm and ST types revealed the heterogenic nature of the strains circulating in Malaysian hospitals. Continuous epidemiological monitoring by molecular typing methods is warranted to improve the management strategies of GAS infections in future.

**Keyword:** Malaysia; *Streptococcus*; Multilocus eqsquence typing; Macrolides